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| 10/581,413 | 06/23/2006 | Kenya Shitara | Q107168 | 1999 |

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| EXAMINER | |
|---|---|
| WEN, SHARON X | |

| ART UNIT | PAPER NUMBER |
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| 1644 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/581,413 | SHITARA ET AL. | |
| | Examiner | Art Unit | |
| | SHARON WEN | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04/17/2008; 08/28/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *5,6 and 27-46* is/are pending in the application.

4a) Of the above claim(s) *45 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6 and 27-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/04/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's amendment, filed 04/17/2008, has been entered.
Claims 1-4 and 7-26 have been canceled.
Claims 27-46 have been added.
Claims 5-6 and 27-46 are pending.

### *Election/Restrictions*

2. Applicant's election of G-CSF in the reply filed on 08/28/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Upon further consideration, the search has been extended to M-CSF, IL-2, vincristin, cyclophosphamide and methotrexate.

Claims 5-6 and 27-46 are currently under examination as they read on a method for treating a CCR4-expressing tumor comprising administering a recombinant antibody that specifically binds chemokine receptor 4 (CCR4).

3. This Action will be in response to Applicant's Arguments/Remarks, filed 04/17/2008.

The rejections of record can be found in the previous Office Action.

### *Information Disclosure Statement*

4. The information disclosure statements (IDS) submitted on 06/04/2008 is acknowledged and being considered by the examiner.

### *Claim Objections*

5. The previous claim objections have been withdrawn in view of Applicant's amendment to the claims, filed 04/17/2008.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 34, 37, 38, 40 and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

*The following Grounds of Rejection pertain to an antibody with fewer than all 6 CDRs. (claims 37, 38, 40 and 41)*

Applicant's argument has been considered but has not been found convincing essentially for reasons of record.

In response to Applicant's argument that the "art is rife with the use of single chain fragment variable antibodies" therefore the antibody recited in the present claims are enabled, the following is noted:

Single chain antibodies also require both heavy and light chain variable domains comprising all six CDRs for antigen binding.

The breadth of the instant claims, especially in view of the "and/or" language, does not require the antibody to have both heavy and light chain variable domains, thus read on antibody with less than all six CDRs.

The state of the art recognized that all three CDRs of the heavy chain variable region and all three CDRs of the light chain variable region were important for determining the ability of the antibody to bind antigen. For example, Padlan et al. (PNAS 1989, 86:5938-5942) describe the crystal structure of an antibody-lysozyme complex where all 6 CDRs contribute at least one residue to binding and one residue in the framework is also in contact with antigen (see entire document, but especially page 5940, right column, section under "**Structure of the Combining Site**").

Furthermore, Bendig (Methods: A Companion to Methods in Enzymology 1995; 8:83-93) reviews that the general strategy for "humanizing" antibodies involves the substitution of all six CDRs from a rodent antibody that binds an antigen of interest, and that all six CDRs are involved in antigen binding (see entire document, but especially Figures 1-3).

Thus the state of the art recognized that it would be highly unpredictable that an antibody comprising less than all six CDRs from an antibody with a desired specificity would bind the same antigen. Thus the minimal structure which provides the function of CCR4 binding appears to include six CDRs (three in the heavy chain variable region and three in the light chain variable region) from the same antibody.

The specification as filed provides no working examples showing that fewer than all six CDRs are required for binding to CCR4. Neither does the specification appear to provide sufficient guidance as to which subsets of CDRs could be used in an antibody comprising less than all six CDRs from an antibody having CCR4-binding specificity and still maintain CCR4 binding. Without sufficient guidance, it would require undue experimentation of the skilled artisan to make antibodies or antigen-binding fragments thereof which could bind CCR4 that comprised fewer than all six CDRs from a parental antibody that bound CCR4.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant's argument has not been found persuasive.

Therefore, the rejection of record is maintained, as it applies to the amended and newly added claims. The rejection of record is incorporated by reference herein, as if reiterated in full.

The new references used are necessitated by Applicant's argument to support the same grounds of rejection.

*The following Grounds of Rejection pertain to biological deposit. (claim 34)*

Applicant's argument has been considered but has not been found convincing essentially for reasons of record.

In response to Applicant's argument that the specification provides the sequences for the heavy and light chain variable region, thus the deposit is not required to practice the invention, it is noted that claim 34 is drawn to an antibody that reacts with the epitope bound by the monoclonal antibody produced by KM 2160 hybridoma. Therefore, the hybridoma is required to practice the claimed invention.

As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line or hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Although applicant has deposited hybridoma clone KM2160 on August 12, 2004 with the International Patent Organism Depository, National Institute of Advanced Industrial Science and Technology, AIST Tsukuba Central 6, 1-1, Higashi 1-chome Tsukuba-shi, Ibaraki, Japan, and accorded Accession Number FERM BP-10090 (see page 11 of the specification) there appears no assurances indicated above. Applicant's provision of these assurances would obviate this rejection.

Applicant's argument has not been found persuasive.

Therefore this rejection is maintained.

***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 5-6 and 27-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Shitara et al. (US 2003/0175273 A1, see entire document).

Applicant's argument has been considered but has not been found convincing essentially for reasons of record and reiterated herein Applicant's convenience.

> Shitara et al. teach a method comprising administering a medicament comprising a combination of a recombinant anti-CCR4 antibody and a pharmaceutically active agent, wherein the agent is G-CSF (see, e.g., paragraphs [0159]-[0163] and [0229]-[0251]).
>
> In particular, the reference antibody appears to be the same or nearly the same antibody as the instant application with identical CDRs (see paragraphs [0049]-[0050] and SEQ ID NOs: 1-3 and 5-7). In addition, the reference teaches the antibody to be is a human chimeric antibody or a human CDR-grafted antibody (see abstracted and paragraph [0310]). Furthermore, the reference teach a monoclonal antibody produced by hybridoma KM2160 (see paragraph [0255]-[0258]).
>
> Given the same or nearly the same antibody, the reference antibody would inherently bind to positions 13 to 25 of amino acid of CCR4 of SEQ ID NO: 1 and would not have an activity of inhibiting binding of TARC or MDC as a CCR4 ligand to CCR4.
>
> There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

In response to Applicant's argument that the prior art did not teach or suggest administering the antibody and agent as independent components, it is noted that the present claims do not require the antibody and the agent to be independent components. Given the open language of "comprising" and under the broadest reasonable interpretation, the antibody conjugated to an agent read on the present claim.

In addition to G-CSF as the agent, the prior art also taught M-CSF, IL-2, vincristine, cyclophosphamide and methotrexate (see paragraph [0162]-[0163]).

Furthermore, the prior art taught using the same or nearly the same antibody to treat cancer, specifically leukemia or lymphomatosis, which reads on hematopoietic organ tumor (see claims 43-46). Therefore, the prior art anticipated all limitations of the present claims.

Applicant's argument has not been found persuasive.

Therefore, the rejection of record is maintained, as it applies to the amended and newly added claims. The rejection of record is incorporated by reference herein, as if reiterated in full.

***Conclusion***

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571)272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Examiner, Art Unit 1644
December 3, 2008

/Phillip Gambel/
Phillip Gambel
Primary Examiner
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Art Unit 1644
December 8, 2008